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GAGCTCGGAT CCACTACTCG ACCACGCGT CCGGCCAGGA CCTCTGTGAA CCGGTCGGGG 60

CGGGGGCCGC CTGGCCGGGA GTCTGCTCGG CCGTGGGTGG CCGAGGAAGG GAGAGAACGA 120

TCGCGGAGCA GGGCGCCCGA ACTCCGGGCG CCGCGCC ATG CGC CGG GCC AGC CGA 175
Met Arg Arg Ala Ser Arg
1 5

GAC TAC GGC AAG TAC CTG CGC AGC TCG GAG GAG ATG GGC AGC GGC CCC 223
Asp Tyr Gly Lys Tyr Leu Arg Ser Ser Glu Glu Met Gly Ser Gly Pro
10 15 20

GGC GTC CCA CAC GAG GGT CCG CTG CAC CCC GCG CCT TCT GCA CCG GCT 271
Gly Val Pro His Glu Gly Pro Leu His Pro Ala Pro Ser Ala Pro Ala
25 30 35

CCG GCG CCG CCA CCC GCC GCC TCC CGC TCC ATG TTC CTG GCC CTC CTG 319
Pro Ala Pro Pro Pro Ala Ala Ser Arg Ser Met Phe Leu Ala Leu Leu
40 45 50

FIG.1A

GGG CTG GGA CTG GGC CAG GTG GTC TGC AGC ATC GCT CTG TTC CTG TAC	367
Gly Leu Gly Leu Gly Gln Val Val Cys Ser Ile Ala Leu Phe Leu Tyr	
55 60 65 70	
TTT CGA GCG CAG ATG GAT CCT AAC AGA ATA TCA GAA GAC AGC ACT CAC	415
Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Ser Thr His	
75 80 85	
TGC TTT TAT AGA ATC CTG AGA CTC CAT GAA AAC GCA GGT TTG CAG GAC	463
Cys Phe Tyr Arg Ile Leu Arg Leu His Glu Asn Ala Gly Leu Gln Asp	
90 95 100	
TCG ACT CTG GAG AGT GAA GAC ACA CTA CCT GAC TCC TGC AGG AGG ATG	511
Ser Thr Leu Glu Ser Glu Asp Thr Leu Pro Asp Ser Cys Arg Arg Met	
105 110 115	
AAA CAA GCC TTT CAG GCG GCC GTG CAG AAG GAA CTG CAA CAC ATT GTG	559
Lys Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val	
120 125 130	

FIG.1B

GGG CCA CAG CGC TTC TCA GGA GCT CCA GCT ATG ATG GAA GGC TCA TGG	607
Gly Pro Gln Arg Phe Ser Gly Ala Pro Ala Met Met Glu Gly Ser Trp	
135 140 145 150	
TTG GAT GTG GCC CAG CAG CGA GGC AAG CCT GAG GCC CAG CCA TTT GCA CAC	655
Leu Asp Val Ala Gln Arg Gly Lys Pro Glu Ala Gln Pro Phe Ala His	
155 160 165	
CTC ACC ATC AAT GCT GCC AGC ATC CCA TCG GGT TCC CAT AAA GTC ACT	703
Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser Gly Ser His Lys Val Thr	
170 175 180	
CTG TCC TCT TGG TAC CAC GAT CGA GGC TGG GCC AAG ATC TCT AAC ATG	751
Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Ala Lys Ile Ser <u>Asn</u> Met	
185 190 195	

FIG.1C

ACG TTA AGC AAC GGA AAA CTA AGG GTT AAC CAA GAT GGC TTC TAT TAC	799
Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln Asp Gly Phe Tyr Tyr	
200 205 210	
CTG TAC GCC AAC ATT TGC TTT CGG CAT CAT GAA ACA TCG GGA AGC GTA	847
Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Ser Val	
215 220 225 230	
CCT ACA GAC TAT CTT CAG CTG ATG GTG TAT GTC GTT AAA ACC AGC ATC	895
Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr Val Lys Thr Ser Ile	
235 240 245	
AAA ATC CCA AGT TCT CAT AAC CTG ATG AAA GGA GGG AGC ACG AAA AAC	943
Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly Gly Ser Thr Lys <u>Asn</u>	
250 255 260	
TGG TCG GGC AAT TCT GAA TTC CAC TTT TAT TCC ATA AAT GTT GGG GGA	991
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly	
265 270 275	

FIG.1D

TTT	TTC	AAG	CTC	CGA	GCT	GGT	GAA	GAA	ATT	AGC	ATT	CAG	GTG	TCC	AAC	1039
Phe	Phe	Lys	Leu	Arg	Ala	Gly	Glu	Glu	Ile	Ser	Ile	Gln	Val	Ser	<u>Asn</u>	
280						285					290					
CCT	TCC	CTG	CTG	GAT	CCG	GAT	CAA	GAT	GCG	ACG	TAC	TTT	GGG	GCT	TTC	1087
Pro	Ser	Leu	Leu	Asp	Pro	Asp	Gln	Asp	Ala	Thr	Tyr	Phe	Gly	Ala	Phe	
295					300					305						310
AAA	GTT	CAG	GAC	ATA	GAC	T	GAGACTCATT	TCGTGGAACA	TTAGCATGGA							1136
Lys	Val	Gln	Asp	Ile	Asp											
																315
TGTCCTAGAT	GTTTGGAAC	TTCTTAAAA	ATGGATGATG	TCTATACATG	TGTAAGACTA											1196
CTAAGAGACA	TGGCCCACGG	TGTATGAAAC	TCACAGCCCT	CTCTCTTGAG	CCTGTACAGG											1256
TTGTGTATAT	GTAAGTCCA	TAGGTGATGT	TAGATTCATG	GTGATTACAC	AACGGTTTAA											1316

FIG.1E

CAATTTTGT	ATGATTTCCT	AGAATTGAAC	CAGATTGGGA	GAGTATTCC	GATGCTTATG	1376
AAAAACTTAC	ACGTGAGCTA	TGGAAGGGG	TCACAGTCTC	TGGGTCTAAC	CCCTGGACAT	1436
GTGCCACTGA	GAACCTTGAA	ATTAAGAGGA	TGCCATGTCA	TTGCAAAGAA	ATGATAGTGT	1496
GAAGGGTTAA	GTTCTTTTGA	ATTGTTACAT	TGCGCTGGGA	CCTGCAAATA	AGTTCCTTTT	1556
TTCTAATGAG	GAGAGAAAAA	TATATGTATT	TTTATATAAT	GTCTAAAGTT	ATATTTCAGG	1616
TGTAATGTTT	TCTGTGCAAA	GTTTTGTAAA	TTATATTGT	GCTATAGTAT	TTGATTCAAA	1676
ATATTTAAAA	ATGTCTCACT	GTTGACATAT	TTAATGTTTT	AAATGTACAG	ATGTATTTAA	1736
CTGGTGCACT	TTGTAATTCC	CCTGAAGGTA	CTCGTAGCTA	AGGGGCAGA	ATACTGTTTC	1796
TGGTGACCAC	ATGTAGTTTA	TTTCTTTATT	CTTTTAACT	TAAAGAGTC	TTCAGACTTG	1856

FIG.1F

TCAAAACTAT GCAAGCAAAA TAAATAAATA AAAATAAAAT GAATACCTTG AATAATAAGT	1916
AGGATGTTGG TCACCAGGTG CCTTTCAAAT TTAGAAGCTA ATTGACTTTA GGAGCTGACA	1976
TAGCCAAAAA GGATACATAA TAGGCTACTG AAATCTGTCA GGAGTATTTA TGCAATTATT	2036
GAACAGGTGT CTTTTTTTAC AAGAGCTACA AATTGTAAAT TTTGTTTCTT TTTTTTCCCA	2096
TAGAAAATGT ACTATAGTTT ATCAGCCAAA AAACAATCCA CTTTTTAATT TAGTGAAAGT	2156
TATTTTATTA TACTGTACAA TAAAAGCATT GTCTCTGAAT GTTAATTTT TGGTACAAA	2216
AATAAATTG TACGAAAACC TGAAAAAAA AAAAAAAGG CGGCCGCTCT	2276
AGAGGGCCCT ATTCTATAG	2295

FIG.1G

FIG.2A

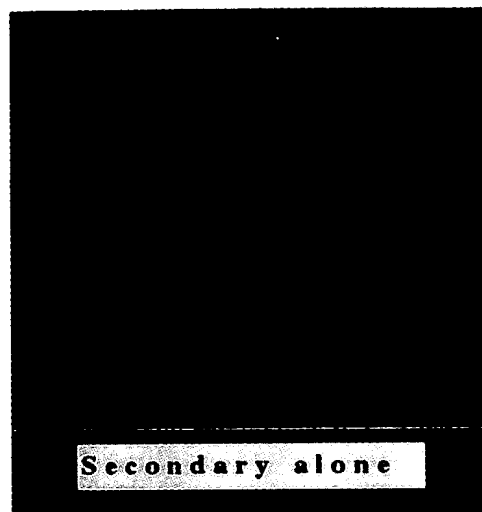


FIG.2B

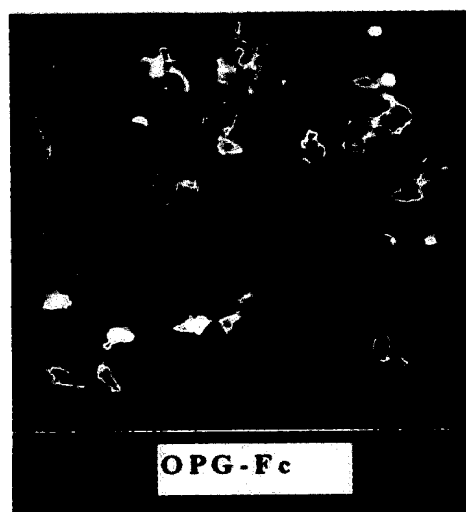
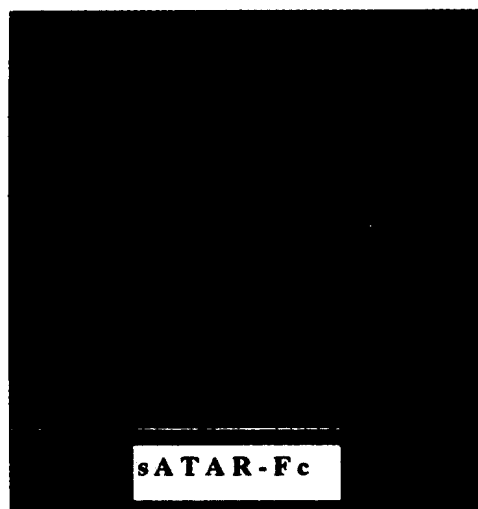


FIG.2C



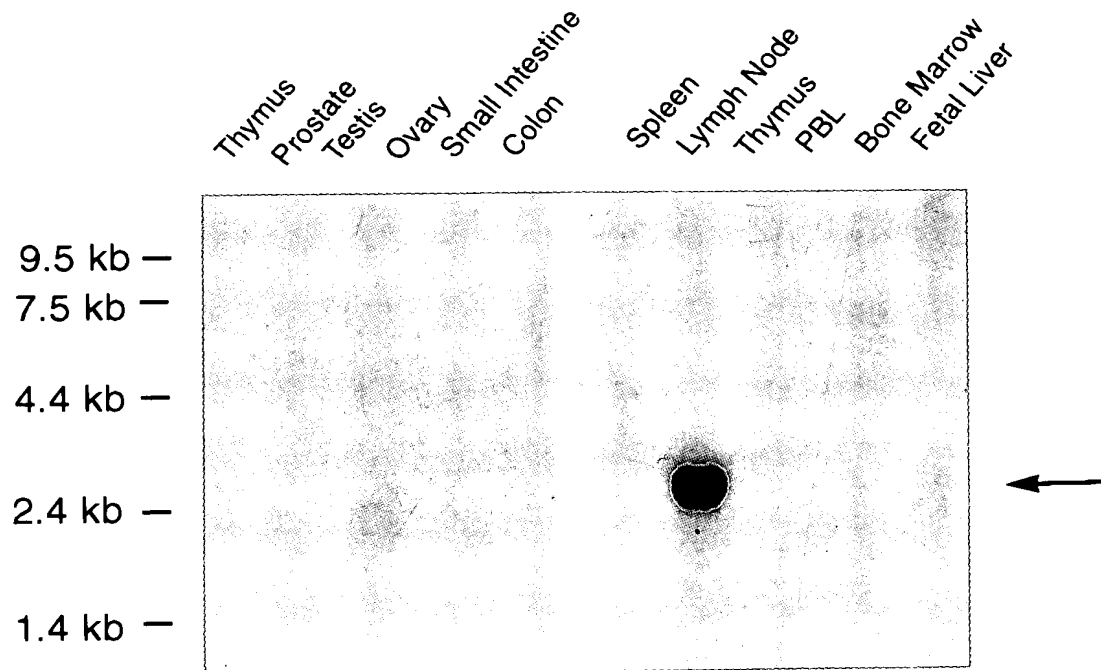


FIG.3

10 30 50
AAGCTTGATACCGAGCTCGGATCCACTACTCGACCCACGCTCCGGCGCCCGAGAGCC

70 90 110
AAAGCCGGCTCCAAAGTCGGCGCCCACTCGAGGCTCCGCCCGCAGCCTCCGGAGTTGGC

130 150 170
CGCAGACAAGAAGGGAGGGAGCGGGAGAGGGAGAGAGCTCCGAAGCAGAGGCCGAG

190 210 230
CGCCATGCCCGCGCCAGCAGAGACTACACCAAGTACCTGCGTGGCTCGGAGAGATGGG
M R R A S R D Y T K Y L R G S E M G

250 270 290
CGCGGGCCCCGGAGCCCCGACGAGGGCCCCCTGCACGCCCGCCGCTGCGCCGCA
G G P G A P H E G P L H A P P P A P H

310 330 350
CCAGCCCCCGCGCTCCCGCTCCATGTTCGTGGCCCTCCTGGGGCTGGGGCTGGGCCA
Q P P A A S R S M F V A L L G L G L G Q

370 390 410
GGTTGTCTGCAGGTCGCCCTGTCTTCTATTTCAGAGCGCAGATGGATCCTAATAGAAT
V V C S V A L F F Y F R A Q M D P N R I

FIG.4A

430 450 470
ATCAGAAGATGGCACTCACTGCATTATAGAAATTTTGAGACTCCATGAAATGCAGATTT
S E D G T H C I Y R I L R L H E N A D F

490 510 530
TCAAGACAACTCTGGAGAGTCAAGATACAAATTAATACCTGATTCATGTAGGAGAAT
Q D T T L E S Q D T K L I P D S C R R I

550 570 590
TAAACAGGCCCTTTCAAGGAGCTGTGCAAAAGGAATTACAACATATCGTTGGATCACAGCA
K Q A F Q G A V Q K E L Q H I V G S Q H

610 630 650
CATCAGAGCAGAGAAAGCGATGGTGGATGGCTCATGGTTAGATCTGGCCAAAGAGGAGCAA
I R A E K A M V D G S W L D L A K R S K

670 690 710
GCTTGAAGCTCAGCCCTTTTGCTCATCTCACTATTAATGCCACCGACATCCCATCTGGTTC
L E A Q P F A H L T I N A T D I P S G S

730 750 770
CCATAAAGTGAGTCTGTCCTCTTGGTACCATGATCGGGGTGGGCCAAAGATCTCCAACAT
H K V S L S S W Y H D R G W A K I S N M

FIG.4B

790 810 830
GACTTTTAGCAATGGAAACTAATAGTTAATCAGGATGGCTTTTATTACCTGTATGCCAA
T F S N G K L I V N Q D G F Y Y L Y A N

850 870 890
CATTTGCTTTCGACATCATGAACCTTCAGGAGACCTAGCTACAGAGTATCTTCAACTAAT
I C F R H H E T S G D L A T E Y L Q L M

910 930 950
GGTGACGTCACTAAACCCAGCATCAAAATCCCAAGTTCTCATACCCCTGATGAAAGGAGG
V Y V T K T S I K I P S S H T L M K G G

970 990 1010
AAGCACCAAGTATTGGTCAGGGAATTCTGAATTCCATTTTATTCCATAAACGTTGGTGG
S T K Y W S G N S E F H F Y S I N V G G

1030 1050 1070
ATTTTTTAAGTTACGGTCTGGAGAGGAAATCAGCATCGAGGTCTCCAAACCCCTCTTACT
F F K L R S G E E I S I E V S N P S L L

1090 1110 1130
GGATCCGGATCAGGATGCAACATACTTTGGGGCTTTTAAAGTTCGAGATATAGATTGAGC
D P D Q D A T Y F G A F K V R D I D

FIG.4C

```
1150          1170          1190
CCCAGTTTGGAGTGTATGTATTCCCTGGATGTTTGGAAACATTTTAAACAAGCC

1210          1230          1250
AAGAAAGATGTATATAGGTGTGTGAGACTACTAAGAGGCATGGCCCCAACGGTACACGAC

1270          1290          1310
TCAGTATCCATGCTCTTGACCTTGTAGAGAACACCGCGTATTTACAGCCAGTGGGAGATGT

1330          1350          1370
TAGACTCATGGTGTACACAATGGTTTTTAAATTTTGTAATGAATTCCTAGAATTAAA

1390          1410          1430
CCAGATTGGAGCAATTACGGGTGACCTTATGAGAACTGCATGTGGGCTATGGGAGGGG
```

FIG.4D

1450 1470 1490
TTGGTCCCTGGTCATGTGCCCCCTTCGCAGCTGAAGTGGAGAGGGTGTCATCTAGCGCAAT

1510 1530 1550
TGAAGGATCATCTGAAGGGGCAAAATCTTTTGAATTGTTACATCATGCTGGAACCTGCAA

1570 1590 1610
AAAATACTTTTCTAATGAGGAGAGAAATAATATGTATTTTATATAATATCTAAAGTTA

1630 1650 1670
TATTTCAGATGTAATGTTTCTTTCTTGCAGAGTATTGTAAATTATATTGTGCTATAGTATT

1690 1710 1730
TGATTCAAAATATTTAAAAATGCTCTTGCTGTGACATATTTAATGTTTAAATGTACAGA

1750 1770 1790
CATATTTAACTGGTGCACTTTGTAAATTCCTGGGAAACTTGCAGCTAAGGAGGGGAA

1810 1830 1850
AAAAATGTTGTTCCCTAATATCAAAATGCAGTATATTCTTCGTTCTTTTAAAGTTAATAG

FIG.4E

1870	1890	1910
ATTTTTCAGACTTGTCAGCCTGTGCAAAAAATTAAATGGATGCCCTTGAATAAAG		
1930	1950	1970
CAGGATGTTGGCCACCAGGTGCCTTTTCAAAATTTAGAACTAATTGACTTTAGAAAGCTGA		
1990	2010	2030
CATTGCCAAAAGGATACATAATGGGCCACTGAAATCTGTCAAGAGTAGTTATATAATTG		
2050	2070	2090
TTGAACAGGTGTTTTTCCACAAGTGCCGCAAAATTGTACCTTTTTTTTTTCAAAATAG		
2110	2130	2150
AAAAGTTATTAGTGGTTATCAGCAAAAAGTCCAAATTTAATTAGTAAATGTTATCTT		
2170	2190	2210
ATACTGTACAATAAAAACATTGCCCTTTGAAATGTTAATTTTTTGGTACAAAAATAATTTA		
2230	2250	2270
TATGAAAAAAAAGGGCGCGCTCTAGAGGGCCCTATTCTATAG		

FIG.4F

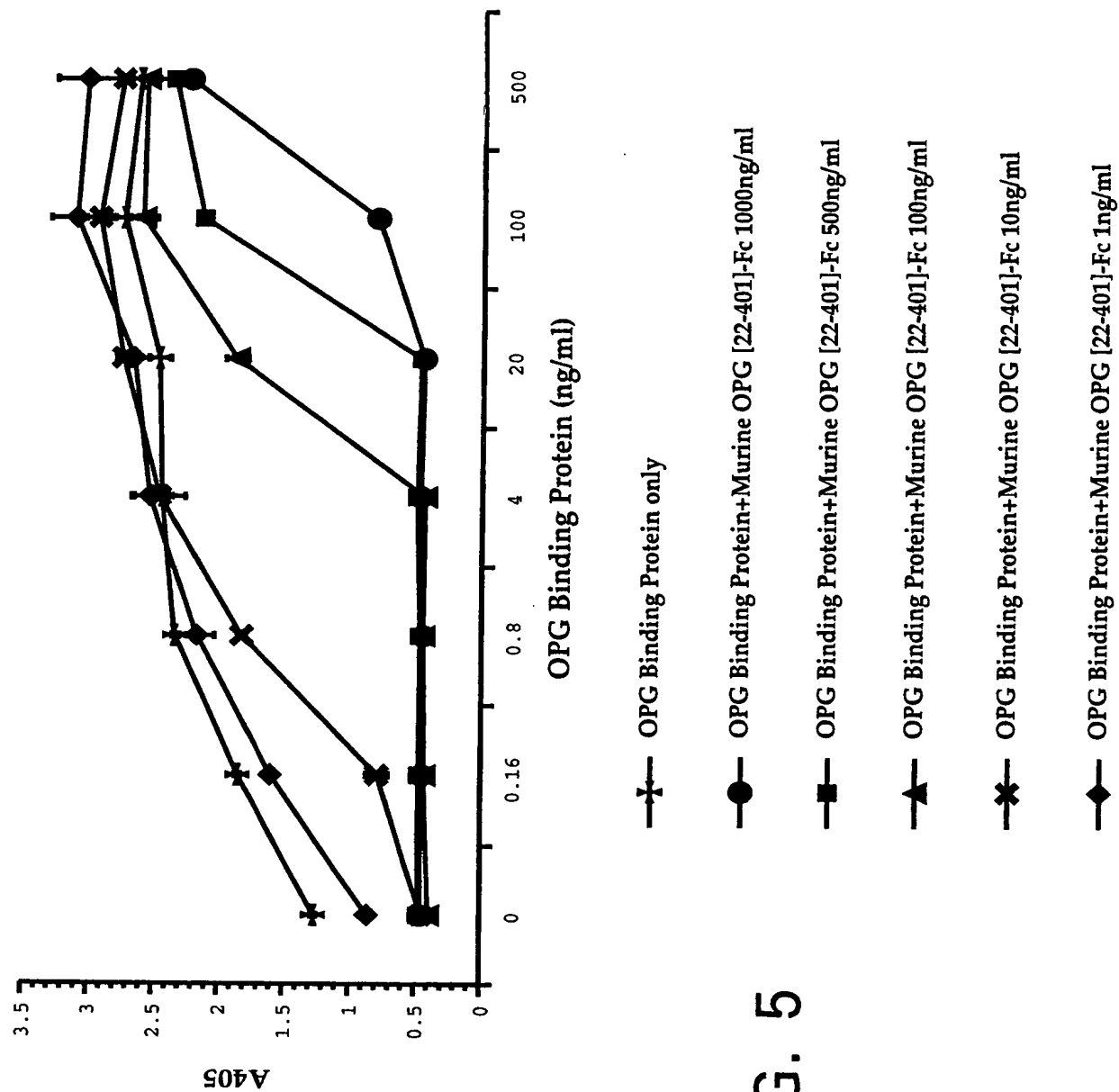


FIG. 5

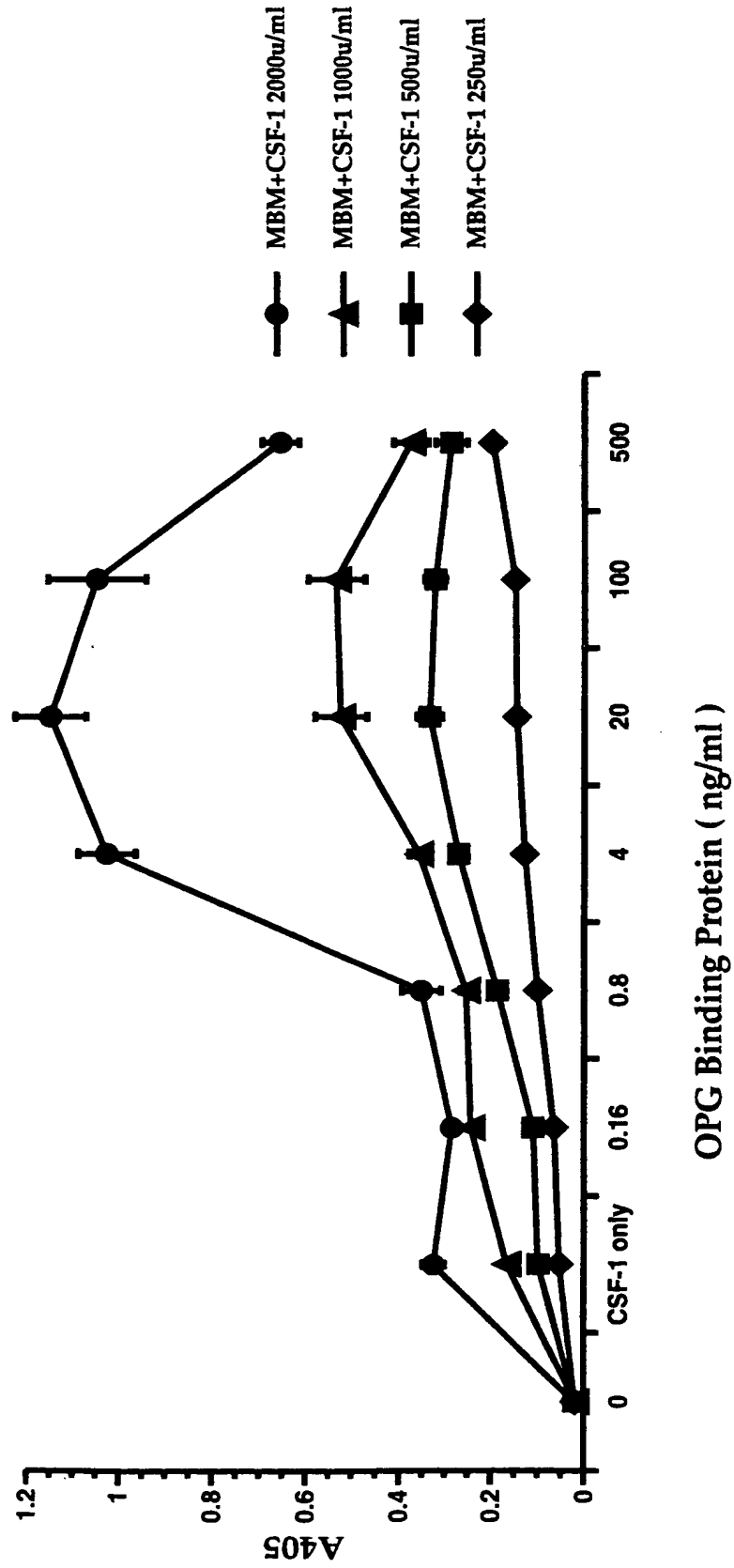


FIG. 6

FIG.7A

Toluidine Blue Staining



TRAP staining



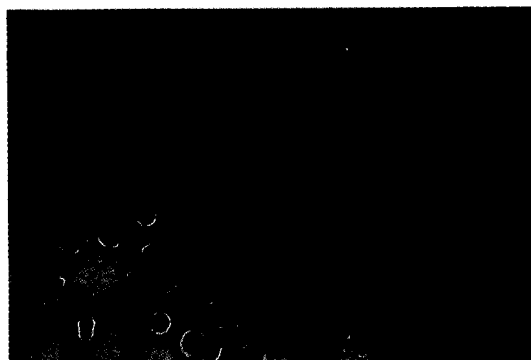
Bone Marrow Cells + M-CSF-1

FIG.7B

Toluidine Blue Staining



TRAP staining



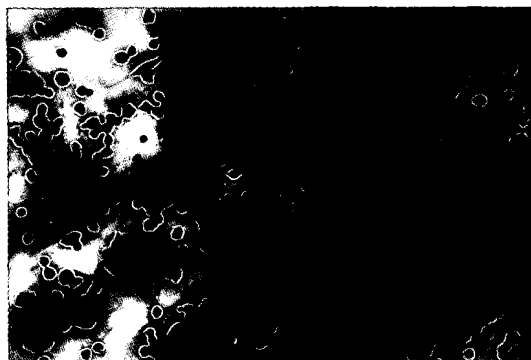
Bone Marrow Cells + OPG Binding Protein

FIG.7C

Toluidine Blue Staining



TRAP staining



Bone Marrow Cells + M-CSF-1 + OPG Binding Protein

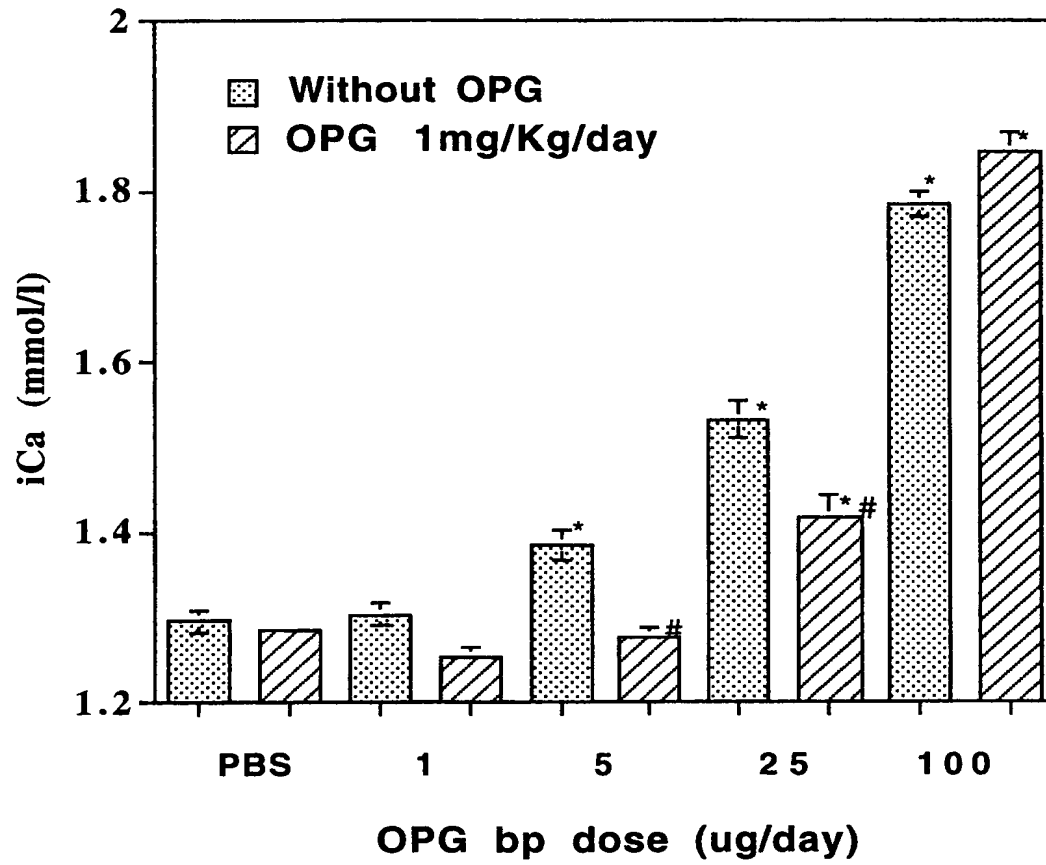


FIG. 8

PBS

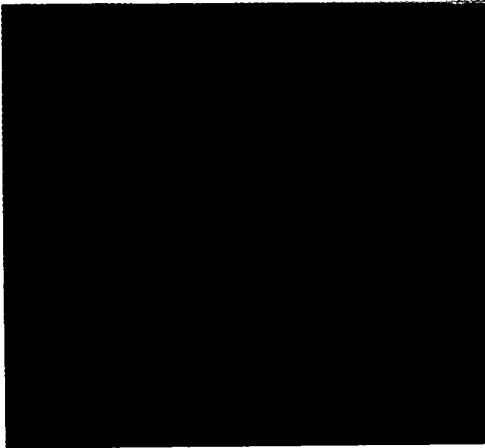


FIG.9A

OPGbp 5ug/d



FIG.9B

OPGbp 25ug/d

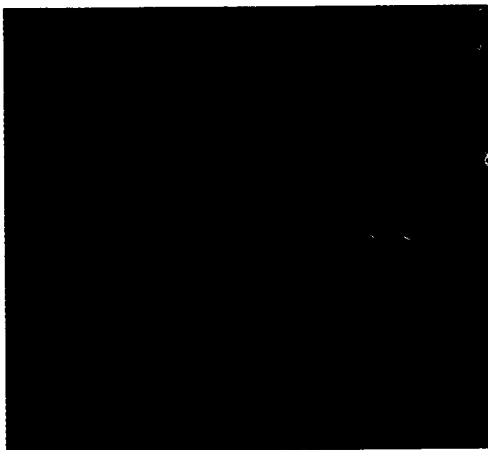


FIG.9C

OPGbp100ug/d



FIG.9D

10 30 50
ACTGACCCACGCGTCCGCCGCCGCCGACCCGCGCCATGGACCCGCGCGCGCGCGCGCC
70 90 110
GCCAGCTGCCCGCGCGTGTGGCGCTCTGCGTGTCTGCTGCTGCTCCACTGCAGGTGACTC
Q L P A P L L A L C V L L V P L Q V T L
130 150 170
TCCAGGTCACTCCTCCATGCACCCAGGAGAGGCATTATGAGCATCTCGGACGGTGTGCA
Q V T P P C T Q E R H Y E H L G R C C S
190 210 230
GCAGATGCCGAACCAGGAAAGTACCTGTCTCTTAAGTGCACCTCCTACCTCCGACAGTGTGT
R C E P G K Y L S S K C T P T S D S V C
250 270 290
GTCTGCCCTGTGGCCCCGATGAGTACTTGGACACCTGGAATGAAGAAGATAAATGCTTGC
L P C G P D E Y L D T W N E E D K C L L
310 330 350
TGCATAAAGTCTGTGATGCAGGCAAGGCCCTGGTGGCGGTGGATCCTGGCAACACACGG
H K V C D A G K A L V A V D P G N H T A

FIG.10A

370 390 410
CCCCGCGTCGCTGTGCTTGCACGGCTGGCTACCACTGGAACCTCAGACTGCCAGTGTGCTGCC
P R R C A C T A G Y H W N S D C E C C R
430 450 470
GCAGGAACACGGAGTGTGCACCTGGCTTCGGAGCTCAGCATCCCTTGCAGCTCAACAAGG
R N T E C A P G F G A Q H P L Q L N K D
490 510 530
ATACGGTGTGCACACCCCTGCCCTCCCTGGGCTTCTTCAGATGTCTTTTCGTCCACAGACA
T V C T P C L L G F F S D V F S S T D K
550 570 590
AATGCCAAACCTTGGACCAACTGCACCCCTCCTTGGAAGCTAGAAGCACACACCGGGACAA
C K P W T N C T L L G K L E A H Q G T T
610 630 650
CGGAATCAGATGTGGTCTGCAGCTCTTCCATGACACTGAGGAGACCAACCAAGGAGGCC
E S D V V C S S S M T L R R P P K E A Q

FIG.10B

670 690 710
AGGCTTACCTGCCAGTCTCATCGTTCTGTGCTCCTCTTTCATCTCTGTGGTAGTAGTGGCTG
A Y L P S L I V L L L L F I S V V V V A A
730 750 770
CCATCATCTTCGGCGTTTACTACAGGAAGGAGGAAAGCGCTGACAGCTAATTGTGGA
I I F G V Y Y R K G G K A L T A N L W N
790 810 830
ATTGGTCAATGATGCTTGCAGTAGTCTAAGTGGAATAAGGAGTCCTCAGGGACCGTT
W V N D A C S S L S G N K E S S G D R C
850 870 890
GTGCTGGTTCCCACTCGGCAACCTCCAGTCAGCAAGAAGTGTGGAAGGTATCTTACTAA
A G S H S A T S S Q Q E V C E G I L L M
910 930 950
TGA CTGGGAGGAGAAGATGGTTCCAGAACGACGGTGCTGGAGTCTGTGGCCCTGTGTGTG
T R E E K M V P E D G A G V C G P V C A
970 990 1010
CGGCAGGTGGGCCCTGGCAGAAAGTCAGAGATTCTAGGACGTTACACTGGTCAGCGAGG
A G G P W A E V R D S R T F T L V S E V

FIG.10C

1030 1050 1070
TTGAGACGCAAGGAGACCTCTCGAGGAAGATTCCACAGAGATGAGTACACGACCGGC
E T Q G D L S R K I P T E D E Y T D R P
1090 1110 1130
CCTCGCAGCCTTCGACTGGTTCACTGCTCCTAATCCAGCAGGAAGCAAATCTATACCCC
S Q P S T G S L L L I Q Q G S K S I P P
1150 1170 1190
CATTCAGGAGCCCTGGAAGTGGGGGAGAACGACAGTTTAAGCCAGTGTTCACCGGGA
F Q E P L E V G E N D S L S Q C F T G T
1210 1230 1250
CTGAAAGCACGGTGGAATTCTGAGGGCTGTGACTTCACTGAGCCTCCGAGCAGAACTGACT
E S T V D S E G C D F T E P P S R T D S
1270 1290 1310
CTATGCCCGTGTCCTGAAAGCACCTGACAAAGAAATAGAAGGTGACAGTTGCCCTCC
M P V S S P E K H L T K E I E G D S C L P
1330 1350 1370
CCTGGGTGGTCAGCTCCAACTCAACAGATGGCTACACAGGCAGTGGGAACACTCCTGGGG
W V V S S N S T D G Y T G S G N T P G E

FIG.10D

1390 1410 1430
AGGACCATGAACCCCTTTCCAGGGTCCCTGAAATGTGGACCATTGCCCCCAGTGTGCTACACA
D H E P F P G S L K C G P L P Q C A Y S
1450 1470 1490
GCATGGGCTTTCCCAAGTGAAGCAGCAGCCAGCATGGCAGAGCGGGAGTACGGCCCCAGG
M G F P S E A A A S M A E A G V R P Q D
1510 1530 1550
ACAGGGCTGATGAGAGGGAGCCTCAGGGTCCGGAGCTCCCCAGTGACCAGCCACCTG
R A D E R G A S G S G S P S D Q P P A
1570 1590 1610
CCTCTGGGAACGTGACTGGAAACAGTAACTCCACGTTTCATCTCTAGCGGGCAGGTGATGA
S G N V T G N S N S T F I S S G Q V M N
1630 1650 1670
ACTTCAAGGGTGACATCATCGTGGTGTATGTACGCCAGACCTCGCAGGAGGCCCCGGGTT
F K G D I I V V Y V S Q T S Q E G P G S
1690 1710 1730
CCGCAGAGCCCGAGTCGGAGCCCGTGGGCCGCCCTGTGCAGGAGGAGACGCTGGCACACA
A E P E S E P V G R P V Q E E T L A H R

FIG.10E

```
1750          1770          1790
GAGACTCCTTTGCGGCACCGCGCCGCGCTTCCCGACGTCGTGCCACCGGGGCTGGGC
  D S F A G T A P R F P D V C A T G A G L
1810          1830          1850
TGCAGGAGCGGGCACCCCGGCAGAGGACGGGACATCGCGGCCGGTGCAGGAGCAGG
  Q E Q G A P R Q K D G T S R P V Q E Q G
1870          1890          1910
GTGGGCGCAGACTTCACCTCCATACCCAGGGTCCGGACAATGTGCAGAAATGACCTCACC
  G A Q T S L H T Q G S G Q C A E
1930          1950          1970
TTCTCTGTCTGCCCTGGGTGCAGGGCACCCAGTGCCCTTCCAAAACATGGTGTAGCTAGC
1990          2010          2030
CACTGTGCACCTCCTCACTGGTGCAGGCTGCTGGCATGGTGATGGAGCCCACCTCTCACT
2050          2070
TCCTCCAGTGCCCCCTCTCCTCTGCGCTCCTAC
```

FIG.10F

FIG.11A

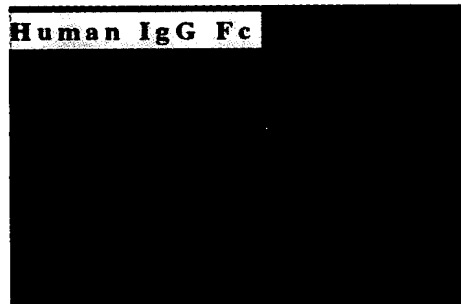
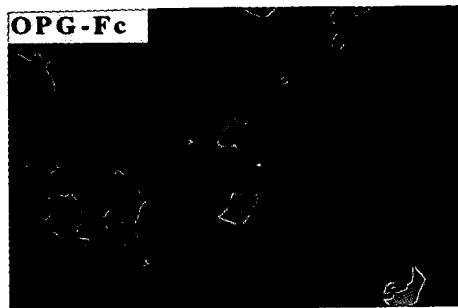


FIG.11B



FIG.11C



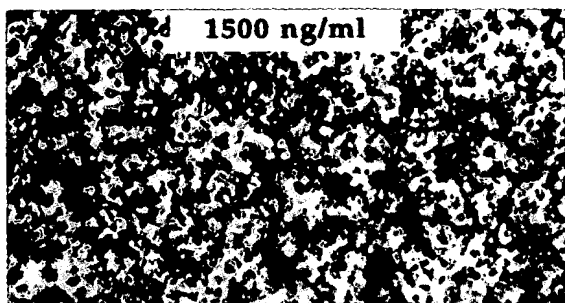


FIG.12A

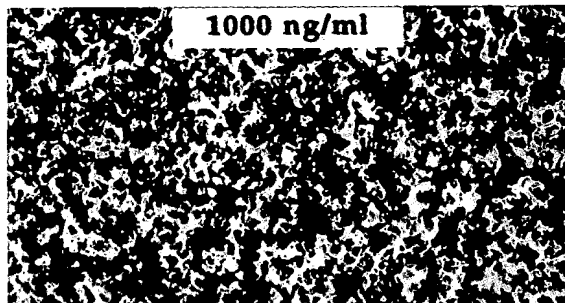


FIG.12B

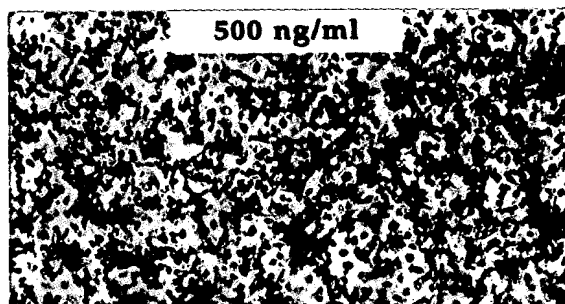


FIG.12C

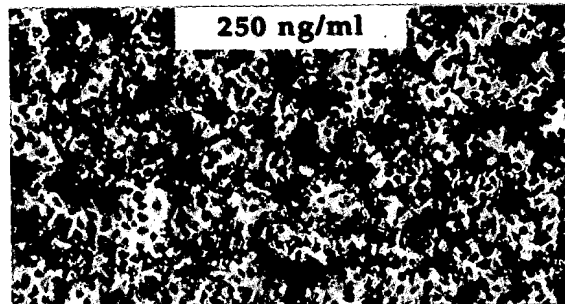


FIG.12D

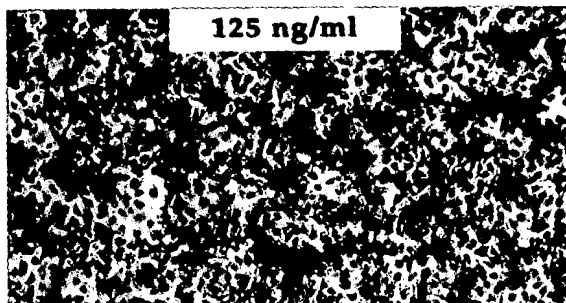


FIG.12E

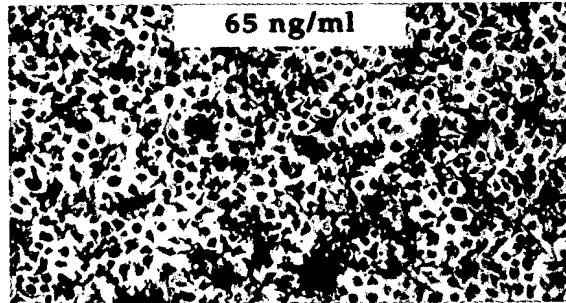


FIG.12F

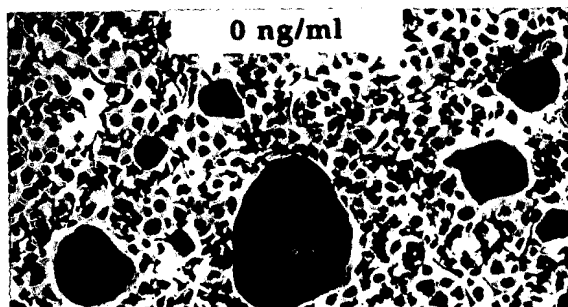
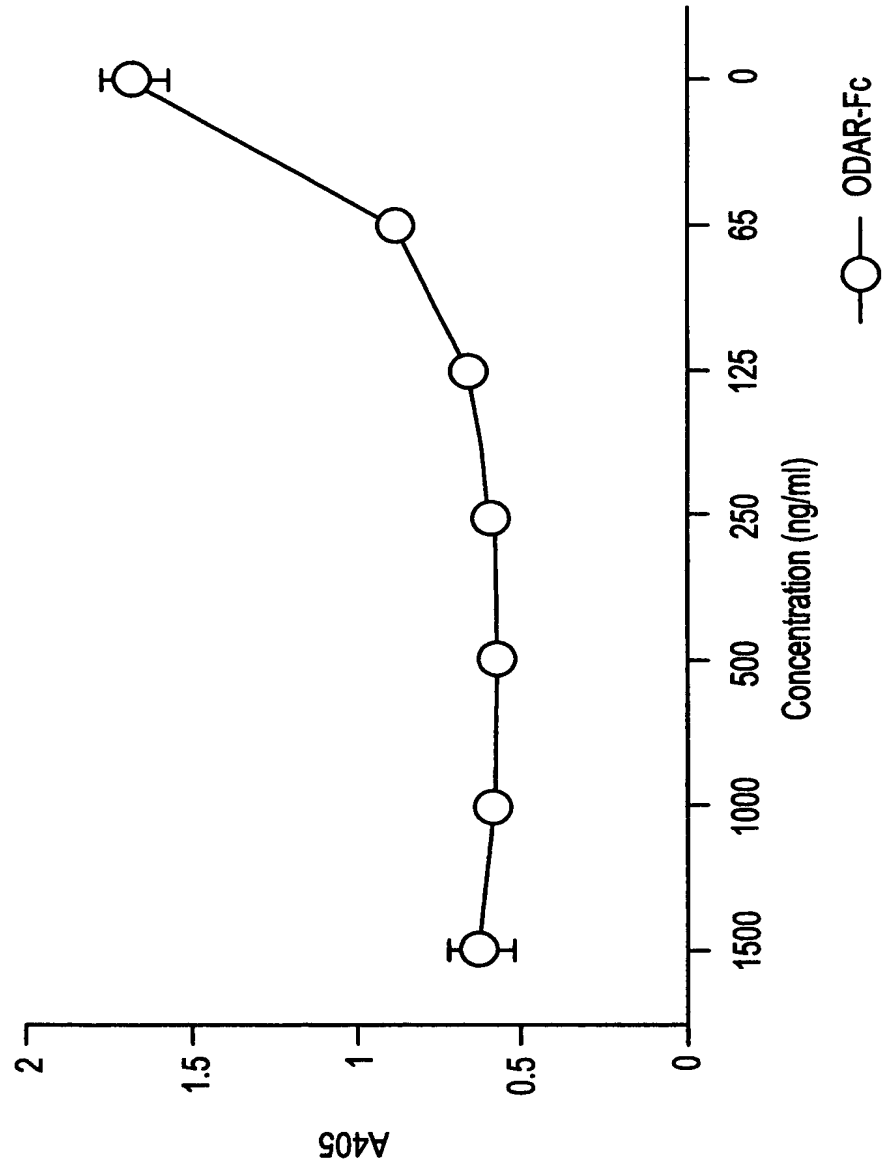
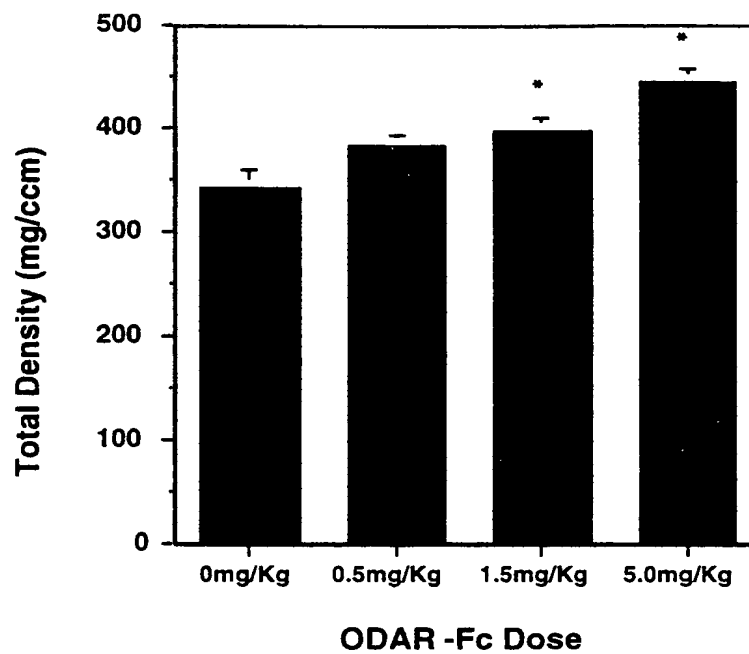


FIG.12G

FIG. 12H





* Different to vehicle treated control $p < 0.05$.

FIG.13